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Symposium Overview

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The Life Sciences Research Office (LSRO) of the Federation of American Societies for Experimental Biology (FASEB), provides scientific assessments of topics in the biomedical sciences. Reports are based upon comprehensive literature reviews and the scientific opinions of knowledgeable investigators engaged in specific areas of biology and medicine.

The extrapolation of data on carcinogenic responses of animal models to estimations of risk of cancer in humans is a complex and controversial subject. The quantity of test substance responsible for the carcinogenic response is an inherent aspect of the process of risk assessment. There are two phases of evaluating dose response in the contemporary approach to risk assessment: dose-range extrapolation and dose scaling. Dose-range extrapolation involves the estimation of low doses and their effects from high-dose exposures based on mathematical models of the dose-response function. Dose scaling is the process of interspecies conversion of dose-response data to equipotent doses for humans. Regulatory agencies have adopted several different strategies for interspecies dose scaling. As examples, the U.S. Environmental Protection Agency (EPA) computes the human equipotent dose in proportion to the 0.67 power of body mass, while the Food and Drug Administration (FDA) uses the first power of body mass for computations of permissible intakes of food additives and a constant fraction in the diet for permissible concentrations of residues in food.

Numerous investigators, publications, and symposia have explored mathematical-statistical models from which dose-range extrapolations of carcinogenic risk are derived. In contrast, little has been published on the subject of dose scaling of carcinogenic potency. In addition, there have been few comprehensive reviews on the principles, applications, or limitations of dose scaling. The increasing use of alternative test systems in applied toxicology and findings from alternative approaches such as molecular genetics and pharmacokinetics present the need for redefining criteria for scaling carcinogenic potency. Regulatory agencies are being required to evaluate information that is either nontraditional (e.g., data from studies of tissue cultures and isolated genetic material) or conflicting (e.g., data indicating different effects from alternate animal models and/or from animal models and cellular systems). The merits of integrating alternative approaches to risk assessment in regulatory practice will require continuing evaluation.

The Life Sciences Research Office, Federation of American Societies for Experimental Biology, under a contract from the Center for Food Safety and Applied Nutrition, FDA, prepared a comprehensive review and assessment of biological bases for interspecies extrapolation of carcinogenicity data (*1*). The papers in this volume of *Environmental Health Perspectives* are a compilation of manuscripts presented at a symposium on January 6, 1986, in Bethesda, Maryland.

Members of the ad hoc Panel on Interspecies Extrapolation of Carcinogenicity Data met twice to obtain background information, review data analyses, and discuss related subjects. Authors of the symposium manuscripts and members of the ad hoc Panel reviewed interim drafts of these papers and provided additional documentation and viewpoints for incorporation into the symposium proceedings.

LSRO acknowledges the support of FDA and the participation of an ad hoc Panel on Interspecies Extrapolation of Carcinogenicity Data, Willard J. Visek, Chairman; Ralph C. Wands, Cochairman; symposium speakers Edward J. Calabrese, David B. Clayson, James E. Gibson, Dante G. Scarpelli, Thomas J. Slaga, Frank G. Standaert, and Thomas B. Starr; and symposium discussion panel members Byron E. Butterworth, Robert L. Dedrick, John C. Kirschman, Ian C. Munro, Joseph V. Rodricks, Elizabeth K. Weisburger, Richard M. Welch, and Christopher F. Wilkinson. The report was edited by Thomas A. Hill, Ralph C. Wands, and Richard W. Leukroth, Jr.

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Inquiries regarding invited papers at the symposium (Part B) and workshop discussions (Part A) should be directed to the Life Sciences Research Office, FASEB, Bethesda, MD 20814.

REFERENCE

1. Hill, T. A., Wands, R. C., and Leukroth, R. W., Jr., Eds. Biological Bases for Interspecies Extrapolation of Carcinogenicity Data. Federation of American Societies for Experimental Biology, Special Publications Office, Bethesda, MD, 1986.